REMARKS

The presently claimed invention features nucleic acid molecules related to a nucleic acid molecule derived from a strain of *Xenorhabdus bovienii*. The nucleic acid molecules encode polypeptides that are toxic to certain nematodes. The previous claims were mis-numbered because claim 58 was missing. The claims have been renumbered as suggested by the examiner. No new matter has been added.

Applicants appreciate the notification that claims 53-55 and 65 are allowable.

Rejections Under 35 U.S.C. §112, first paragraph (written description)

The Examiner rejected claims 57-64 and 66-70 as allegedly failing to meet the written description requirement of 35 U.S.C. §112, first paragraph.

The Examiner objected to the hybridization conditions previously recited in claim 57. The Examiner stated that the specification does not support application of the recited hybridization conditions to SEQ ID NO:23 or to nucleic acid molecules that encode a polypeptide having at least 70% identity to SEQ ID NO:23. Applicants have amended the claims to delete the reference to hybridization conditions.

Present claim 57 is drawn to an isolated nucleic molecule comprising a nucleotide sequence encoding a polypeptide having an amino acid sequence that is at least 85% identical to SEQ ID NO:23, wherein the polypeptide is toxic to a nematode. Thus, the nucleic acid molecules of this claim and the claims dependent thereon include limitations related to: (a) the homology of the amino acid sequence of the polypeptide encoded by the nucleic acid molecule to a specific polypeptide (SEQ ID NO:23) and (b) the function of the polypeptide encoded by the nucleic acid molecule (toxicity to nematodes). In *Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1559 (Fed. Cir. 1997) the court stated that the written description requirement can be met by either a disclosure of a sufficient number of species within the claimed genus or a combination of structural and functional limitations. Thus, present claim 57 meets the standards set forth in *Lilly*.

In *Ex parte Sun* (Appeal No. 2003-1993; copy enclosed) The Board of Patent Appeals and Interferences considered the appropriateness of rejections under the written description and enablement requirements for claims similar to those presently pending. In *Ex parte Sun* the Board explained that the following claim was illustrative of those on appeal.

> 31. An isolated wee1 nucleic acid molecule comprising a member selected from the group consisting of:
>
> (a) a polynucleotide that encodes a polypeptide of SEQ ID NO:2;
>
> (b) a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1;
>
> (c) a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1; and
>
> (d) a polynucleotide complementary to a polynucleotide of (a) through (c).

The specification disclosed that SEQ ID NO:2 encodes a protein having a defined function (similar to that of a known tyrosine kinase). The specification explained that the protein is useful in genetic engineering of corn plants to increase productivity. The examiner rejected claim 31 as failing to meet the written description requirement, arguing that one skilled in the art could not predict the structure and function of nucleic acid "comprising a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1" The examine also argued that the specification did not "teach a single representative species with 80% identity and WEE1 function".

After reviewing the relevant case law, including *Lilly* and *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316 (Fed. Cir. 2002), the Board concluded that the rejected claims, including claim 31, met the written description requirement. The Board pointed out that the specification describes the sequence of a nucleic acid molecule encoding SEQ ID NO:2 and the sequence of a nucleic acid molecule comprising the coding sequence of SEQ ID NO:1. The Board also noted that the specification provides an example of how to screen for WEE1 activity. The Board concluded that,

> [I]t would reasonably appear that such a description in the specification would constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with *Enzo*.
>
> In our view, the examiner has failed to indicate why one of ordinary skill in the art, who is in possession of the very specific chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, would be unable to recognize, upon reading the disclosure, that appellants invented the claimed subject matter, including homologues sharing structural features with the specifically claimed and disclosed structures.

Thus, it can be seen that claims similar to those in the present application have been found to meet the written description standards set forth in *Lilly* and *Enzo*. In the present case, as in *Ex parte Sun*, only a single species is disclosed. In the present case, as in *Ex parte Sun*, a functional assay is provided. It should be pointed that specification of the application considered by the Board did indicate a small region of the WEE1 gene likely to be important for activity. The present specification (see page 36 and Figure 4H) identified the insertion point tn26 as reducing the toxicity of p14-2f (SEQ ID NO:23) towards nematodes. Thus, the present specification identifies a functionally important region of SEQ ID NO:23.

It is clear that a single species combined with a functional assay can provide an adequate written description for a claim to a genus of nucleic acid molecules. In view of the forgoing, Applicants request that the rejections based on the written description requirement of 35 U.S.C. §112, first paragraph be withdrawn.

Rejections Under 35 U.S.C. §112, first paragraph (enablement)

The Examiner rejected previously pending claims 57-64 and 66-70 as allegedly failing to meet the enablement requirement of 35 U.S.C. §112, first paragraph.

Present claim 53 and certain claims dependent on claim 53 are drawn to an "isolated nucleic molecule comprising a nucleotide sequence encoding a polypeptide having an amino acid sequence that is at least 85% identical to SEQ ID NO:23, wherein polypeptide is toxic to a nematode.

Regarding the previously pending claims, the Examiner argued the number of potential peptides having at least 70% identity to a reference polypeptide the length of SEQ ID NO:23 is very large and that it would be unreasonable to screen all such polypeptides to identify those toxic to nematodes. Present claim 57 require that the claimed nucleic acid molecule encode a polypeptide having an amino acid sequence that is at least 85% identical to SEQ ID NO:23 and that is toxic to a nematode

As noted previously, the specification teaches straight forward assay for determining whether a nucleic acid molecule encodes a polypeptide that in toxic to a nematode (see pages 31-37 of the specification). Briefly, the assay entails introducing the nucleic acid into a expression vector to create an expression construct that is used to transform *E. coli* that are grown in multi-well culture dishes to generate a library of clones. *C. elegans* larvae are added to the *E. coli* cultures and the cultures are visually examined several days later to assess nematode development. Thus, the assay is well suited to high throughput library screening. Indeed, high throughput library screening was used to initially identify cHRIM5 as a clone encoding a polypeptide(s) toxic to a nematode (see page 31 of the specification).

Given the teachings of the specification, one skilled in the art could make and use the nucleic acids without undue experimentation because the specification teaches one skilled in the art how to identify nucleic acid molecules encoding biologically active polypeptides. The Court of Appeals for the Federal Circuit has identified eight factors that must be considered in determining whether undue experimentation would be required to practice a claimed invention: "(1) the quantity of experimentation necessary, (2) the amount and direction of guidance provided, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *In re Wands*, 858 F.2d 731, 740 (Fed. Cir.1988).

With respect to the relative skill in the art, it is clear that the relative skill in art of generating variant polypeptides is very high. For example, those skilled in the art are aware of various random mutagenesis protocols can be used to create libraries of clones encoding variant polypeptides.

With respect to the guidance provided by the specification, by providing a simple, high throughput screening method, the specification provides considerable guidance in the generation and screening of variant polypeptides.

With respect to the absence or presence of working examples, the specification provides a working example of successful high throughput screening for the identification of nucleic acids encoding toxic peptides.

Regarding the breadth of the claims, it is Applicants' position that the claims are not excessively broad encompassing as they do nucleic acid molecules that both encode polypeptides having at least 80% identity to a reference sequence and hybridize under quite stringent conditions to a particular nucleic acid molecule.

With respect to predictability, although it cannot always be predicted whether a given amino acid change will alter function, it is generally understood, despite some exceptions, that certain types of variants, e.g., those involving conservative amino acid substitutions are more likely to retain function.

With respect to the amount of experimentation required, the high through-put screening methods described in the present specification are capable of testing many, many peptides very rapidly. There are two reasons for this. First, the assay itself is quite simple in so much as it involves simply exposing nematodes to a clone expressing the polypeptide of interest. Second, as of the priority date of the present application, 1999, technology was available to rapidly generate large libraries of variant polypeptides.

In *Ex parte Sun*, discussed in greater detail above, the Board concluded that the rejected claims, including claim 31, were enabled. In this regard the Board noted that the specification provided both an activity assay and the identification of at least one region likely to be important for WEE1 activity. Here an activity assay is provided. In addition, as discussed above, the present specification (see page 36 and Figure 4H) identifies insertion point tn26 as reducing the toxicity of p14-2f (SEQ ID NO:23) towards nematodes. Thus, the present specification identifies a functionally important region of SEQ ID NO:23. In view of these teachings and the Wands factors analyzed above, Applicants submit that the present claims are enabled.

In view of the forgoing, Applicants respectfully request that the enablement rejections under 35 U.S.C. §112, first paragraph be withdrawn.

Rejections Under 35 U.S.C. §112, second paragraph

The Examiner rejected claim 67 (now claim 66) as indefinite for reciting "claim 53 for claim 57". Applicants have amended claims 66 to recite "claim 53 or claim 57". In view of this amendment, Applicants request that this rejection be withdrawn.

Rejections Under 35 U.S.C. §102(b)

The Examiner rejected claim 56 as anticipated by Thiele et al. (Eur. J. Epidemol. 10:413, 1995). The Examiner argued that claim 56 is anticipated because Thiele et al. discloses a polypeptide that includes a 6 amino acid sequence found in SEQ ID NO:23. In making this rejection the Examiner stated that "claim 56 reads on a portion of the nucleotide sequence of SEQ ID NO:52, wherein the portion comprises a nucleotide sequence encoding a polypeptide of any size from the amino acid sequence of SEQ ID NO:22 and 23" (emphasis added). Applicants believe that the Examiner has mis-read claim 56. The claim reads as follows:

> 56. An isolated nucleic acid molecule comprising a portion of the nucleotide sequence of SEQ ID NO:52, the portion comprising:
> a) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:22; and
> b) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:23.

Thus, claim 56 is drawn to as isolated nucleic acid molecule that includes a portion of SEQ ID NO:52. However, the portion of SEQ ID NO:52 includes both: (a) a sequence encoding a polypeptide comprising SEQ ID NO:23 and (b) a sequence encoding a polypeptide comprising SEQ ID NO:22. Thus, the nucleic acid molecule must have a portion that encodes at least the entirety of SEQ ID NO:23 and a portion that encodes at least the entirety of SEQ ID NO:23.

Properly understood, claim 56 cannot be anticipated by Thiele et al. This is because, according to the Examiner, Thiele et al. discloses a polypeptide includes only six contiguous amino acids of SEQ ID NO:23. In view of this, Applicants respectfully request that the rejection under 35 U.S.C. §102(b) be withdrawn.

Conclusion

Applicants respectfully request that the rejections be withdrawn and the pending claims allowed. Enclosed is a Petition for Extension of Time with the appropriate fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 19 OCT 2005

Anita L. Meiklejohn, Ph.D.
Reg. No. 35,283

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

Paper No. 27

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte YUEJIN SUN, BRIAN R. DILKES, BRIAN A. LARKINS, KEITH S. LOWE, WILLIAM J. GORDON-KAMM and RICARDO A. DANTE

Appeal No. 2003-1993
Application No. 09/470,526

ON BRIEF

Before WILLIAM F. SMITH, MILLS and GRIMES, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 2-11, 31, 33 and 35-36 which are the claims on appeal in this application. Claims 14, 32 and 37 have been allowed.

Claim 31 is illustrative of the claims on appeal and reads as follows:

31. An isolated wee1 nucleic acid comprising a member selected from the group consisting of:
(a) a polynucleotide that encodes a polypeptide of SEQ ID NO:2.;
(b) a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1;

(c) a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1; and
(d) a polynucleotide complementary to a polynucleotide of (a) through (c).

The prior art references relied upon by the examiner are:

Aligue et al. (Aligue), "Regulation of *Schizosaccharomyces pombe* Wee1 Tyrosine Kinase," J. Biol. Chem., Vol. 272, pp. 13320-13325 (1997)

Hemerly et al. (Hemerly), "Dominant negative mutants of the Cdc2 kinase uncouple cell division from iterative plant development," The EMBO Journal, Vol. 14, pp. 3925-3936 (1995)

Grounds of Rejection

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

These rejections are reversed.

DISCUSSION

In reaching our decision in this appeal, we have given consideration to the appellants' specification and claims, to the applied references, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the noted rejections, we make reference to the examiner's Answer for the examiner's reasoning in support of the rejection, and to the appellants' Brief for the appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

Background

The subject matter of the present application is generally directed to corn plant nucleic acids and their encoded proteins which are involved in cell cycle regulation. Specification, page 4. In particular, the claimed invention is directed to a wee1 homologue from maize, zmwee1, whose activity resembles related protein tyrosine kinases. Specification, page 6. The zmwee1 protein is indicated in the specification to be useful in the genetic engineering of the corn plant to increase maize productivity. Specification, page 3.

More specifically, claim 31 is directed to an isolated wee1 nucleic acid comprising a member selected from the group consisting of: a polynucleotide that encodes a polypeptide of SEQ ID NO:2.; a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1; a polynucleotide comprising the

coding sequence set forth in SEQ ID NO:1; and a polynucleotide complementary to a polynucleotide described above.

According to the prior art, Aligue, Wee1 tyrosine kinase regulates mitosis by carrying out the inhibitory tyrosine 15 phosphorylation of Cdc2 M-phase inducing kinase. Abstract. The specification confirms this, stating "induced wee1 overexpression results in phosphorylation of p34 at tyrosine-15 (inactivating p34), effectively blocking the transition from G2 into mitosis." Specification, page 37. The "encoded [wee1] protein is an important part of the checkpoint control machinery that regulates $p34^{cdc2}$ activity and it's [sic] participation in the active MPF (maturation promoting factor) complex." Specification, page 36. Wee1 activity can be stimulated by the CDK2-cyclin A complex, or inhibited by nim1. Specification, page 36.

Description

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

The Federal Circuit has discussed the application of the written description requirement of the first paragraph of § 112 to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court explained that

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus . . . [H]owever, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id.

The Lilly court also stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. at 1567, 43 USPQ2d at 1405. Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id. at 1568, 43 USPQ2d at 1406.

The Federal Circuit has also addressed the written description requirement in the context of DNA-related inventions. See Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'showing that an invention is complete by disclosure of **sufficiently detailed, relevant identifying characteristics** . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" [Emphasis added] Id. at 1324, 63 USPQ2d at 1613 .

The court in Enzo adopted its standard from the USPTO's Written Description Examination Guidelines. See 296 F.3d at 1324, 63 USPQ2d at 1613 (citing the Guidelines). The Guidelines apply to proteins as well as DNAs.

Finally, it is well-settled that the written description requirement of 35 U.S.C. § 112, first paragraph, can be satisfied without express or explicit disclosure of a later-claimed invention. See, e.g., In re Herschler, 591 F.2d 693, 700, 200 USPQ 711, 717 (CCPA 1979): "The claimed subject matter need not be described in haec verba to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented processes including

those limitations." (citations omitted). See also Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue.").

We apply the relevant law above to the facts before us. In the present case, the examiner argues that the "specification does not set forth what specific structural or physical features define the claimed isolated nucleic acids and transgenic cells, plants and seeds." Answer, page 4. The examiner argues that one skilled in the art "could not predict the structure and function of isolated nucleic acids comprising a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 or a polynucleotide complementary thereto, or cells, plants and seeds transformed therewith. The physical features of the claimed isolated nucleic acids and transgenic cells, plants, and seeds cannot be ascertained in the absence of information about the functional activities of these nucleic acids. Additionally, the specification does not disclose the effect of incorporating the claimed isolated nucleic acids into the genome of a cell or plant." Id.

We find the examiner's argument that one skilled in the art could not predict the structure and function of isolated nucleic acids comprising a wee1 to be confusing in the context of a written description rejection, as predictability is not the legal standard or test for such rejections. However, as best we can understand the examiner's argument, the examiner appears to argue that the specification does not describe a wee1

polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

The examiner argues that "Applicant's [sic] own specification fails to teach a single representative species with 80% identity and WEE1 function." Answer, page 5.

We do not agree with the examiner that claim 31 lacks written description in the specification and that appellants were not in possession of the claimed invention at the time the application was filed. First, to satisfy the written description requirement it is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented the claimed subject matter. Thus, we do not find the fact that the specification does not specifically teach the structure of a species with 80% identity and WEE1 function to be dispositive of the written description issue here.

The Enzo court stated that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" Id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Contrary to the examiner's position, it would reasonably appear that such a description in the specification would constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with Enzo (*supra*).

In our view, the examiner has failed to indicate why one of ordinary skill in the art, who is in possession of the very specific chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, would be unable to recognize, upon reading the disclosure, that appellants invented the claimed subject matter, including homologues sharing structural features with the specifically claimed and disclosed structures.

The examiner relies on Aligue for the teaching that amino acids 363-408 of the 550 amino acid N-terminal regulatory domain of *S. pombe* WEE1 are critical to the function of the regulatory domain. The examiner concludes that because "the functional properties of WEE1 and other proteins reside in specific amino acid residues, changes in these residues could have an effect on WEE1 function." Answer, page 5.

We agree with appellants that the examiner has not established with a preponderance of the evidence, that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be altered without disturbing substrate recognition are insufficient to describe a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. What is evident from the record is those of ordinary skill in the art were aware that most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. Those of skill in the art were also aware that the carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis. Thus, those of ordinary skill in the art would have recognized from reading the disclosure that the inventors had invented the isolated wee1 having the specific nucleotide and amino acid sequences and variations of these sequences with mutations in described specific areas of Wee1, while avoiding the introduction of mutations in other regions. This teaching, coupled with the ability to test for functional mutants with the assays provided for in the specification, supports appellants' position that the inventors sufficiently described and were in possession of the invention as claimed, at the time of filing of the patent application.

In our view the examiner has not provided sufficient evidence or analysis to indicate why one of ordinary skill in the art having read the disclosure, would not have been able to recognize that the inventors invented the subject matter within the scope of the claims. The rejection of the claims for lack of written description is reversed.

Enablement

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

It is the examiner's position that the specification is enabling for an isolated wee1 nucleic acid comprising a polynucleotide encoding SEQ ID NO:2 and a polynucleotide comprising SEQ ID NO:1, but does not reasonably provide enablement for a wee1 polynucleotide having 80% identity to the coding region of SEQ ID NO:1. Answer, page 6.

Enablement is a legal determination of whether a patent enables one skilled in the art to make and use the claimed invention, Raytheon Co. v. Roper Corp., 724 F.2d 951, 960, 220 USPQ 592, 599 (Fed. Cir. 1983), and is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive. Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984); W.L. Gore and Associates v. Garlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315 (Fed. Cir. 1983). Nothing more than objective enablement is required, and therefore it is irrelevant

whether this teaching is provided through broad terminology or illustrative examples. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

An analysis of whether the claims under appeal are supported by an enabling disclosure requires a determination of whether that disclosure contained sufficient information regarding the subject matter of the appealed claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie case of lack of enablement, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. See In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). See also In re Morehouse, 545 F.2d 162, 192 USPQ 29 (CCPA 1976).

The threshold step in resolving this issue is to determine whether the examiner has met his burden of proof by advancing acceptable reasoning inconsistent with enablement. "Factors to be considered by the examiner in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman, [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." (footnote

omitted). In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988).

In the present case the examiner provided an analysis of several of the relevant enablement factors on pages 5-9 of the Answer. One of the examiner's primary arguments is that the specification does not disclose any specific structural or functional characteristics of any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. Answer, page 7. The examiner also argues that the "specification does not disclose any examples of how to make a transgenic host cell or plant comprising an isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1" or provide "any definitive evidence that introducing any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 into a plant will result in an alteration of the plant's phenotype." Id.

The examiner relies on Hemerly to support the position that the transformation of plant material is unpredictable in view of the disclosure. According to the examiner, Hemerly teaches "the transformation of *Arabidopsis* and tobacco plants with isolated nucleic acids encoding wild-type and mutant Cdc2a cell cycle regulatory proteins". Answer, page 8. Transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant designed to accelerate the cell cycle unexpectedly did not affect the development of transgenic plants. The transformation of *Arabidopsis* and tobacco with a Cdc2a mutant designed to arrest the cell cycle did affect the development of transgenic plants as expected. Id.

The examiner concludes (Id., pages 8-9)

> Given the unpredictability of determining the function of isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the unpredictability of altering the phenotype of a plant by transforming it with an isolated nucleic acid of SEQ ID NO:1 or isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the absence of guidance in the specification for making and using said nucleic acids and transgenic host cells, plants, and seeds, the lack of working examples, and given the breadth of the claims which encompass multiple polynucleotides having at least 80% identity to the entire coding region of SEQ ID NO:1, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

Analysis of the enablement requirement in the present case dovetails with our analysis with respect to the written description requirement. In particular, the specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Brief, page 9. In addition, the specification page 3, lines 17-31, "describes the level of skill in the art as well as indicating areas of the wee1 gene that can be altered without disturbing substrate recognition." Brief, page 7. Moreover, the specification, page 3, states, "Most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. The carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis."

We agree with appellants that the examiner has not established that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be altered without disturbing substrate recognition are insufficient to enable a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

Nor has the examiner established that one of ordinary skill in the art having the chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1 and the ability to test for expression as described in the specification, would be insufficient to transform cells, plants and seeds in view of the success described in the specification. While the examiner relies on Hemerly for the transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant, the examiner has not explained how or why potential unpredictability associated with Cdc2a expression is related to or affects Wee1 expression. Nor is it clear from the examiner's analysis that the examiner has fully considered the state of the art as it relates to the transformation of vectors, seeds and plant cells, as outlined in the specification.

The Patent and Trademark Office Board of Appeals stated:

> The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Ex parte Jackson, 217 USPQ 804, 807 (1982).

In our view, upon reading the disclosure, those of ordinary skill in the art would have been provided a reasonable amount of guidance to make and use a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. The specification, pages 27-29 outlines methods for transfection and transformation of cells and the introduction of DNA into plants. The examples of the specification indicate successful expression of zmwee1 in E. coli as evidenced by the successful inhibition of cyclin-dependent protein kinase. Specification, pages 33-34. In view of the successful transformation of cells with the disclosed and claimed specific wee1, we find no evidence or sufficient indicated reason of record why one of ordinary skill in the art would not have had a reasonable expectation of success in transforming cells and plant cells with a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 without undue experimentation.

The rejection of the claims for lack of enablement is reversed.

CONCLUSION

The rejection of claims 2-11, 31, 33 and 35-36 under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention is reversed.

The rejection of claims 2-11, 31, 33 and 35-36 under 35 U.S.C. § 112, first paragraph for lack of enablement is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED

WILLIAM F. SMITH Administrative Patent Judge	)
DEMETRA J. MILLS Administrative Patent Judge	) APPEALS AND
	) INTERFERENCES
ERIC GRIMES Administrative Patent Judge	)

Appeal No. 2003-1993
Application No. 09/470,526

PIONEER HI-BRED INTERNATIONAL, INC.
7100 N.W. 62nd Ave.
P.O. Box 1000
Johnson, IA 50131